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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,964	10/12/2000	Geert Maertens	2551-48	5719

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NIXON & VANDERHYE, PC
1100 N GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER
HILL, MYRON G

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/686,964	MAERTENS ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36- 78* is/are pending in the application.

4a) Of the above claim(s) *42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36- 41 and 44- 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 October 2003 has been entered.

Claims 36- 41 and 44- 78 are pending.

Rejections Withdrawn

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 44- 49 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is withdrawn because of the amendment.

Claims 76 and 77 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejections are moot in light of the amendment but see new rejections below.

Claim Rejections - 35 USC § 102

Claims 36- 41, and 50- 78 were rejected under 35 U.S.C. 102(e) as being anticipated by Seidel (US 6036579).

This rejection is withdrawn because of the amendment but it is modified to be a 35 USC § 103, see below.

Claims 39 and 44- 49 were rejected under 35 U.S.C. 102(b) as being anticipated by Leroux-Roels.

This rejection is withdrawn and is modified to be a 35 USC § 103, see below.

Claims 36- 41 and 50 – 77 were rejected under 35 U.S.C. 102(b) as being anticipated by Figard.

The rejection is withdrawn because of amendment.

New or Modified Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44- 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to epitopes comprising at least one amino acid residue selected from the recited group of single amino acids.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. However, a showing of possession alone does not cure the lack of a written description. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 1330, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002).

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). "Compliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.'" *Enzo Biochem*, 296 F.3d at 1324, 63 USPQ2d at 1613.

The specification defines epitope as the following:

As used herein, 'epitope' or 'antigenic determinant' means an amino acid sequence that is immunoreactive. Generally an epitope consists of at least 3 to 4 amino acids, and more usually, consists of at least 5 or 6 amino acids, sometimes the epitope consists of about 7 to 8, or even about 10 amino acids. As used herein, an epitope of a designated polypeptide denotes epitopes with the same amino acid sequence as the epitope in the designated polypeptide, and immunologic equivalents thereof. Such equivalents also include strain, subtype (=genotype), or type group-specific variants, e.g. of the currently known sequences or strains ... or any other newly defined HCV (sub) type. It is to be understood that the amino acids constituting the epitope need not be part of a linear sequence, but may be interspersed by one or more series of any number of amino acids, thus forming a conformational epitope. (page 8, lines 4- 16)

The specification does not disclose the use of single epitopes that comprise one of the recited amino acids.

The specification only uses clones 21 and 32 (from Example 4, 850 bps per clone of coding NS3 gene, about 283 amino acids when translated) that were used in Example 10. Example 9 uses NS3 clones but does not disclose which specific ones were used.

As defined by applicant, it is generally accepted in the art that epitopes consist of 5 or 6 amino acid residues if considered in a linear context. Additionally, as noted by applicant, the epitopes can be conformational and thus require residues that are not in contiguous linear proximity. The definition of epitope as stated above (lines 4- 6) defines epitope as denoting epitope and does not define “immunologic equivalents”.

The definition implies that “newly defined” epitopes, i.e. epitopes that were not known at the time of the invention but known now are encompassed by the definition.

As known in the art and as defined by applicant, an epitope consists of usually 5 or 6 residues. The claims only provide for one amino acid that comprises the epitope.

Applicant has defined the term broadly and one of skill in the art cannot envision epitope fom one single amino acid. Applicant has provided no written description of one epitope that meets the limitations of the claims. Applicant has not taught specific linear or conformational epitopes that comprise the recited residues, or what properties (specific sequences that antibodies bind to) these epitopes have over the many other epitopes in the NS3 polypeptide of HCV. Thus, it is concluded that applicant did not have in their possession the full range of epitopes claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36- 38, 40, 41, and 50- 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. (US 6036579) and Harlow and Lane.

The claims are drawn to a dry solid phase coated with HCV NS3 immunoassay wherein a reducing agent is added in at least one step.

Applicant argues that Seidel et al. at best only teaches reducing agent in the presence of antibody and not as now as now claimed. Also, applicant states that Seidel teaches that the test can be carried out under mild reducing conditions and that applicant has discovered that DTT can be included in the kit.

Applicant's arguments have been fully considered and not found persuasive.

The Office considers a "kit" claim to be a product. That product is what the kit contains/comprises.

Seidel et al. teaches an immunoassay NS3 HCV antigen bound to a solid support and the advantage of using a reducing agent to aid in detection in particular disclosing that antigen with DTT (a reducing agent) to detect anti-HCV antibodies at an earlier time point than without DTT (Example 5). The step at which reducing agent is added and the step of sulphonation/desulphonation are method steps and are not encompassed in the claimed product. The use of fusion protein and type of assay in kit are inherent to the product and obvious to those skilled in the art. There has been no showing that the product claimed by Applicant is any different from the product in the prior art. While Applicant cites a passage in column 4, it is clear from Example 5 that Seidel et al. contemplated an assay using HCV NS3 antigen on a solid support in the presence of reducing agent and that Seidel realized the benefit of using reducing agent allowed for detection of anti-HCV antibodies at an earlier time point.

Seidel et al. does not teach "dry" solid phase.

Harlow and Lane teach in the art of immunoassays and disclose that nitrocellulose can be dried (end of page 607).

It would be obvious to one of ordinary skill in the art at the time of invention that the DTT as taught by Seidel in Example 5 is important to make a more efficient assay because the assay can detect HCV at an earlier time point. The skill in the art of immunoassay is very high and many types of solid phase are known as well as methods of handling. Harlow and Lane show what is known in the art and that is that solid phase

assay components can be dried. One of ordinary skill in that would be motivated to prepare a dry immunoassay so it is ready when needed in a laboratory without having to make the immunoassay each time the assay was done because Harlow and Lane teach that the antigens can last indefinitely when dried on a membrane.

Thus, it would have been *prima facie* obvious to dry the HCV NS3 containing DTT solid phase assay of Seidel as known in the art as taught by Harlow and Lane with the expectation of success.

Claims 39 and 44- 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. (US 6036579) and Harlow and Lane as applied to claims 36- 38, 40, 41, and 44- 76 above, and further in view of Leroux-Roels.

Applicant's argue that the reference does not teach the assay as claimed.

Applicant's arguments have been fully considered and not found persuasive.

Seidel et al. and Harlow and Lane as discussed above teach an assay comprising NS3 antigen in a dry solid phase. Seidel teaches that a range of antegic sequences can be used. The claimed sequence is taught by Leroux-Roels (SEQ ID# 2) is essentially the same as SEQ ID# 18. The sequence of Leroux-Roels contains a initiating methionine residue. For this claimed protein to be expressed it must contain an initiation methionine and therefore it would be obvious to one skilled in the art to add a methionine. The mutations/alternate residues listed in the claims are contained in the alternative residues listed in Fig. 6.

It would be obvious to one of ordinary skill in the art at the time of invention to use the sequences of Leroux-Roels in the assay of Seidel and Harlow and Lane because the sequences are both NS3 and taught to be antigenic.

Thus, it would have been *prima facie* obvious to use the HCV NS3 sequences of Leroux-Roels in a DTT treated solid phase assay of Seidel et al. as modified by Harlow and Lane with the expectation of success.

Claims 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. (US 6036579) and Harlow and Lane as applied to claims 36- 38, 40, 41, and 44- 76 above, and further in view of Icardi et al.

Seidel et al. and Harlow and Lane as discussed above teach an assay comprising NS3 antigen in a dry solid phase.

Seidel et al. and Harlow and Lane do not teach multiple controls or additional antigens.

Icardi et al. teaches an immunoassay, INNO-LIA HCVIII, that contains multiple antigens, HCV core, NS3, 4, and 5, has positive controls, and has a +/- cutoff (page 2332, column 2).

It would be obvious to one of ordinary skill in the art at the time of invention to modify the assay of Seidel and Harlow and Lane to include the features as taught by Icardi et al. because the multiple antigens add specificity and the controls allow determination of how well the test assay worked as taught by Icardi et al.

Thus, it would have been *prima facie* obvious to modify the HCV NS3 DTT treated solid phase assay of Seidel and Harlow and Lane by adding the features of Icardi et al. with the expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
December 6, 2003

JEFFREY STUCKER
PRIMARY EXAMINER